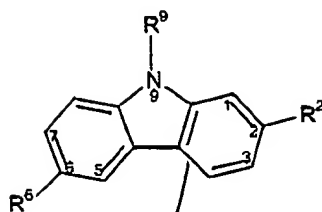
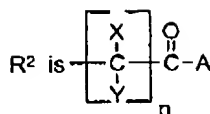


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Formula (I)

wherein:



where A is hydroxy, (C<sub>1</sub> - C<sub>4</sub>)alkoxy, amino, hydroxyamino, mono-(C<sub>1</sub> - C<sub>2</sub>)alkylamino, di-(C<sub>1</sub> - C<sub>2</sub>)alkylamino; X and Y are independently H or (C<sub>1</sub> - C<sub>2</sub>)alkyl; and n is 1 or 2;

R<sup>6</sup> is halogen, (C<sub>1</sub> - C<sub>3</sub>)alkyl, trifluoromethyl, or nitro;

R<sup>9</sup> is H; (C<sub>1</sub> - C<sub>2</sub>)alkyl; phenyl or phenyl-(C<sub>1</sub> - C<sub>2</sub>)alkyl, where phenyl is optionally mono-substituted by fluoro or chloro; -C(=O)-R, where R is (C<sub>1</sub> - C<sub>2</sub>)alkyl or phenyl, optionally mono-substituted by fluoro or chloro; or -C(=O)-O-R<sup>1</sup>, where R<sup>1</sup> is (C<sub>1</sub> - C<sub>2</sub>)alkyl;

where X and Y are different, the (-)(R) and (+)(S) enantiomers thereof; and all pharmaceutically acceptable salt forms, prodrugs and metabolites thereof which are therapeutically active for treating or preventing pain and inflammation,

whereby such pain and inflammation are prevented or alleviated, said side effects are avoided or reduced and COX-2 is selectively inhibited without substantial inhibition of COX-1, the selective inhibition ratio of COX-2 to COX-1 being at least 3:1 based on ex vivo inhibition levels measured in whole blood, with the proviso that said drug is not 6-chloro- $\alpha$ -methyl-9H-carbazole-2-acetic acid.

### Remarks

After entry of this amendment, claims 1, 4, and 15-23 are pending in the present application. Claims 5, 8-14, 24-25 and 26-33 are cancelled without prejudice. Claims 4, 15, 18 and 21 are amended to clarify the claims. No new matter was added by these amendments.

The Examiner has objected to claim 4 and rejected claims 4 and 15-23 under 35 U.S.C. § 112, second paragraph due to claim clarity issues. The present amendments incorporate the

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Examiner's comments. As such, Applicants believe that further and favorable action in the form of a Notice of Allowance Issue is next in order, and such action is earnestly solicited.

Should the Examiner have any questions or comments regarding this amendment or the application in general, he is invited to call the undersigned at (860) 686-0349.

No fee is believed to be due; however, the Commissioner is hereby authorized to charge any extension of time fee, and any other fees that may be required, or credit any overpayment, to Deposit Account No. 16-1445.

Respectfully submitted,  
Pfizer, Inc.

A handwritten signature in black ink, appearing to read "Lisa Samuels", written over the printed name.

Lisa A. Samuels  
Reg. No. 43,080

Pfizer, Inc.  
Eastern Point Road, MS 8260-1611  
Groton, CT 06340

Customer ID No.: 28523

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Exhibit A

5

**MARKED UP CLAIMS**

(strike-through denotes deleted text and underline denotes added text)

4. (Three Times Amended) A method of treating or preventing inflammatory processes and diseases as in Claim 1 further comprising wherein said inhibitory  
 10 compound is used in combination with one or more other therapeutically active agents under the following conditions:

A. where a joint has become seriously inflamed as well as infected at the same time by bacteria, fungi, protozoa, and/or virus, said inhibitory compound is administered in combination with one or more antibiotic, antifungal, antiprotozoal,  
 15 and/or antiviral therapeutic agents;

B. where a multi-fold treatment of pain and inflammation is desired, said inhibitory compound is administered in combination with inhibitors of other mediators of inflammation, comprising one or more members independently selected from the group consisting essentially of:

- 20 1. NSAIDs;
2. H<sub>1</sub>-receptor antagonists;
3. kinin-B<sub>1</sub>- and B<sub>2</sub>-receptor antagonists;
4. prostaglandin inhibitors selected from the group consisting of PGD-, PGF- PGI<sub>2</sub> -, and PGE-receptor antagonists;
- 25 5. thromboxane A<sub>2</sub> (TXA<sub>2</sub>-) inhibitors;
6. 5- and 12-lipoxygenase inhibitors;
7. leukotriene LTC<sub>4</sub> -, LTD<sub>4</sub>/LTE<sub>4</sub> -, and LTB<sub>4</sub> -inhibitors;
8. PAF-receptor antagonists;
9. gold in the form of an aurothio group together with one or more
- 30 hydrophilic groups;
10. immunosuppressive agents selected from the group consisting of cyclosporine, azathioprine, and methotrexate;
11. anti-inflammatory glucocorticoids;
12. penicillamine;
- 35 13. hydroxychloroquine; and

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5                   14. anti-gout agents including colchicine; xanthine oxidase inhibitors  
including allopurinol; and uricosuric agents selected from probenecid, sulfinpyrazone,  
and benzbromarone;

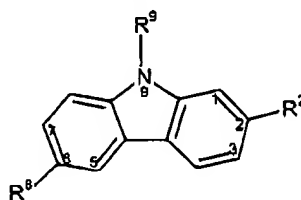
                  C. where older dogs are being treated for disease conditions, syndromes  
and symptoms found in geriatric dogs, said inhibitory compound is administered in  
10 combination with one or more member independently selected from the group  
consisting of:

1. cognitive therapeutics to counteract memory loss and impairment;
2. anti-hypertensives and other cardiovascular drugs intended to  
offset the consequences of atherosclerosis, hypertension, myocardial ischemia,  
15 angina, congestive heart failure, and myocardial infarction, selected from the group  
consisting of:
  - a. diuretics;
  - b. vasodilators;
  - c.  $\beta$ -adrenergic receptor antagonists;
  - 20 d. angiotensin-II converting enzyme inhibitors (ACE-inhibitors),  
alone or optionally together with neutral endopeptidase inhibitors;
  - e. angiotensin II receptor antagonists;
  - f. renin inhibitors;
  - g. calcium channel blockers;
  - 25 h. sympatholytic agents;
  - i.  $\alpha_2$ -adrenergic agonists;
  - j.  $\alpha$ -adrenergic receptor antagonists; and
  - k. HMG-CoA-reductase inhibitors or {anti-hypercholester-oleemics};
3. antineoplastic agents selected from:
  - 30 a. antimitotic drugs selected from:
    - i. vinca alkaloids selected from:
      - [1] vinblastine, and
      - [2] vincristine;
  4. growth hormone secretagogues;
  - 35 5. strong analgesics;
  6. local and systemic anesthetics; and

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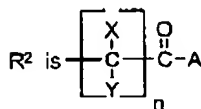
5 7. H<sub>2</sub>-receptor antagonists, proton pump inhibitors, and other  
gastroprotective agents.

15. (Twice Amended) A method of preventing or alleviating pain and  
inflammatory processes and diseases in a member of the species Canis familiaris  
10 with reduced or no undesirable gastro-intestinal side effects normally associated with  
administration to said member of non-steroidal anti-inflammatory drugs, said  
member having been examined by a veterinarian practitioner and diagnosed as in  
need of such treatment using a drug which selectively inhibits inducible cyclo-  
oxygenase-2 (COX-2) to prevent or alleviate said pain and inflammatory processes  
15 with substantially no inhibition of constitutive cyclo-oxygenase-1 (COX-1) to reduce  
or avoid said side effects, which comprises administering to said members of the  
species Canis familiaris that has been so examined and diagnosed an amount  
therapeutically effective to treat or prevent pain and inflammation with reduction in or  
avoidance of said side effects of a drug of the formula:



Formula (I)

wherein:

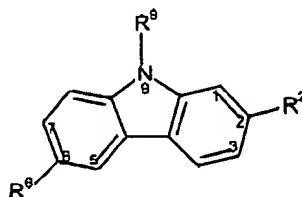


where A is hydroxy, (C<sub>1</sub> - C<sub>4</sub>)alkoxy, amino, hydroxyamino, mono-(C<sub>1</sub> - C<sub>2</sub>)alkylamino,  
25 di-(C<sub>1</sub> - C<sub>2</sub>)alkylamino; X and Y are independently H or (C<sub>1</sub> - C<sub>2</sub>)alkyl; and n is 1 or 2;  
R<sup>8</sup> is halogen, (C<sub>1</sub> - C<sub>3</sub>)alkyl, trifluoromethyl, or nitro;  
R<sup>9</sup> is H; (C<sub>1</sub> - C<sub>2</sub>)alkyl; phenyl or phenyl-(C<sub>1</sub> - C<sub>2</sub>)alkyl, where phenyl is optionally  
mono-substituted by fluoro or chloro; -C(=O)-R, where R is (C<sub>1</sub> - C<sub>2</sub>)alkyl or  
phenyl, optionally mono-substituted by fluoro or chloro; or -C(=O)-O-R<sup>1</sup>,  
30 where R<sup>1</sup> is (C<sub>1</sub> - C<sub>2</sub>)alkyl;

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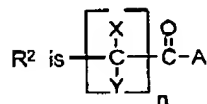
5 where X and Y are different, the (-)(R) and (+)(S) enantiomers thereof; and all pharmaceutically acceptable salt forms, prodrugs and metabolites thereof which are therapeutically active for treating or preventing pain and inflammation, with the proviso that said drug is not 6-chloro- $\alpha$ -methyl-9H-carbazole-2-acetic acid.

10 18. (Twice Amended) A method of treating a member of the species Canis familiaris, which member has been evaluated and determined to be (1) in need of treatment to alleviate or prevent pain and inflammatory processes and diseases with reduced or no undesirable gastro-intestinal side effects normally associated with administration of non-steroidal anti-inflammatory drugs to said member and (2) said  
 15 member will benefit by using such treatment from the selective inhibition of inducible cyclo-oxygenase-2 (COX-2) to prevent or alleviate said pain and inflammatory processes with little or reduced inhibition of constitutive cyclo-oxygenase-1 (COX-1) to reduce or avoid said side effects, comprising administering to said member of the species Canis familiaris which has been so evaluated and diagnosed an amount  
 20 therapeutically effective to treat or prevent pain and inflammation of a drug of the formula:



Formula (I)

wherein:



where A is hydroxy, (C<sub>1</sub> - C<sub>4</sub>)alkoxy, amino, hydroxyamino, mono-(C<sub>1</sub> - C<sub>2</sub>)alkylamino, di-(C<sub>1</sub> - C<sub>2</sub>)alkylamino; X and Y are independently H or (C<sub>1</sub> - C<sub>2</sub>)alkyl; and n is 1 or 2;

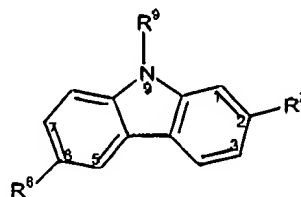
R<sup>6</sup> is halogen, (C<sub>1</sub> - C<sub>3</sub>)alkyl, trifluoromethyl, or nitro;

30 R<sup>9</sup> is H; (C<sub>1</sub> - C<sub>2</sub>)alkyl; phenyl or phenyl-(C<sub>1</sub> - C<sub>2</sub>)alkyl, where phenyl is optionally mono-substituted by fluoro or chloro; -C(=O)-R, where R is (C<sub>1</sub> - C<sub>2</sub>)alkyl or

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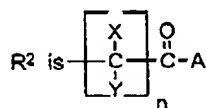
- 5 phenyl, optionally mono-substituted by fluoro or chloro; or  $-C(=O)-O-R^1$ ,  
where  $R^1$  is  $(C_1 - C_2)$ alkyl;  
where X and Y are different, the  $(-)(R)$  and  $(+)(S)$  enantiomers thereof; and all  
pharmaceutically acceptable salt forms, prodrugs and metabolites thereof which are  
therapeutically active for treating or preventing pain and inflammation, with the  
10 proviso that said drug is not 6-chloro- $\alpha$ -methyl-9H-carbazole-2-acetic acid.

21. (Twice Amended) A method of treating a member of the species Canis  
familiaris to prevent or alleviate pain and inflammatory processes and diseases  
which comprises administering to a member of such species which has been  
15 a) evaluated and determined by a veterinarian practitioner to be in need of  
treatment with a drug which inhibits the activity of inducible cyclo-oxygenase-2  
(COX-2) to prevent or alleviate said pain and inflammatory processes while  
b) avoiding or reducing gastro-intestinal side effects normally associated with  
administration of non-steroidal anti-inflammatory drugs to said member and therefore  
20 c) to benefit from treatment with a drug that does not substantially inhibit the  
activity of constitutive cyclo-oxygenase-1 (COX-1) so that said side effects are  
reduced or eliminated,  
which method comprises administering to said member of the species Canis  
familiaris which has been so evaluated and determined, a therapeutically effective  
25 amount of a drug of the formula:



Formula (I)

wherein:



- 30 where A is hydroxy,  $(C_1 - C_4)$ alkoxy, amino, hydroxyamino, mono- $(C_1 - C_2)$ alkylamino,  
di- $(C_1 - C_2)$ alkylamino; X and Y are independently H or  $(C_1 - C_2)$ alkyl; and n is 1 or 2;

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- 5     $R^6$     is halogen,  $(C_1 - C_3)$ alkyl, trifluoromethyl, or nitro;  
      $R^9$     is H;  $(C_1 - C_2)$ alkyl; phenyl or phenyl- $(C_1 - C_2)$ alkyl, where phenyl is optionally  
         mono-substituted by fluoro or chloro;  $-C(=O)-R$ , where R is  $(C_1 - C_2)$ alkyl or  
         phenyl, optionally mono-substituted by fluoro or chloro; or  $-C(=O)-O-R^1$ ,  
         where  $R^1$  is  $(C_1 - C_2)$ alkyl;
- 10   where X and Y are different, the  $(-)(R)$  and  $(+)(S)$  enantiomers thereof; and all  
     pharmaceutically acceptable salt forms, prodrugs and metabolites thereof which are  
     therapeutically active for treating or preventing pain and inflammation,  
     whereby such pain and inflammation are prevented or alleviated, said side effects  
     are avoided or reduced and COX-2 is selectively inhibited without substantial
- 15   inhibition of COX-1, the selective inhibition ratio of COX-2 to COX-1 being at least  
     3:1 based on ex vivo inhibition levels measured in whole blood, with the proviso that  
     said drug is not 6-chloro- $\alpha$ -methyl-9H-carbazole-2-acetic acid.